PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2010/045375	12.08.2010	12.08.2009

International Patent Classification (IPC) or both national classification and IPC
INV. A61K9/16 A61K9/20 A61K9/28 A61K9/50 A61K31/4375 A61P25/14

Applicant
BIOVAIL LABORATORIES INTERNATIONAL (BARBADOS...

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Date of completion of this opinion	Authorized Officer
European Patent Office P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Fax: +31 70 340 - 3016	see form PCT/ISA/210	Glikman, J Telephone No. +31 70 340-3055

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing filed or furnished:

   a. (means)

   ☐ on paper

   ☐ in electronic form

   b. (time)

   ☐ in the international application as filed

   ☐ together with the international application in electronic form

   ☐ subsequently to this Authority for the purposes of search

4. ☐ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	4, 5, 11-18, 20-23, 25-30, 33-67
	No:	Claims	1-3, 6-10, 19, 24, 31, 32
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-67
Industrial applicability (IA)	Yes:	Claims	1-67
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

   and / or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

   see form 210

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1 WO 2007/007105 A1 (CAMBRIDGE LAB IRELAND LTD) 18 January 2007

D2 WO 2006/069030 A1 (COLLEGIUM PHARMACEUTICAL INC) 29 June 2006

D3 WO 2008/079404 A2 (SPHERICS INC) 3 July 2008

D4 WO 2010/018408 A2 (BIOVAIL LAB) 18 February 2010

For document D4, see item VI under

1. Present claims 31-67 relate to methods for treating patients in need of a therapy. Said methods are considered as therapies. The patentability can be dependent upon the formulation of the claims. The EPO, for example, does not recognise as patentable claims to the use of a compound in medical treatment, but may allow claims to a product, in particular substances or compositions for use in a first or further medical treatment.

2. The present application does not meet the criteria of Article 33(2) PCT, because the subject-matter of claims 1-3, 6-10,19, 24, 31-32 is not new:

Document D1 discloses a capsule made of dihydrotetrabenazine with lactose encapsulated in gelatin (see D1, page 65). Insofar as the term "tetrabenazine" of present claim 1 may be understood, it also relates to the tetrabenazine compound of D1: see the present description, page 14, lines 10-11, the term " the tetrabenazine can be... in the form of prodrugs and metabolites". Moreover an encapsulating agent such as gelatin is considered as a "release retarding agent" according to present claim 1 (see item VIII, point 1, under). See also D1, p.24, lines 21-24, where the release delaying agent is a coating agent such as a maleic anhydride copolymer.

Moreover, the comparison with an immediate release composition as in present claim 1 is unclear (see item VIII, point 2 under) and cannot help in distinguishing the present subject-matter from D1

Document D1 is prejudicial to the novelty of the subject-matter of claims 1-3, 6-10, 19, 24, 31-32

3. The present application does not meet the criteria of Article 33(3) PCT, because the subject-matter of claims 1-67 does not involve an inventive step:

3.1 Document D1 is regarded as being the prior art closest to the present subject-matter.

The subject-matter of claims 1-3, 6-10, 19, 24, 31-32 is known from D1 (see point 2 above) and cannot therefore rely on an inventive step in view of D1.

3.2 Dependent claims, the subject-matter of which may appear to be new in view of D1, do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step. The solution proposed in said claims cannot be considered as involving an inventive step (Article 33(3) PCT) for the following reasons:

- It is known to use antidyskinetics in delayed release forms: see also D2, claims 1, 26 (lines 29 on page 48), and claim 30, see D3, page 75, penultimate line and claims 1 and 13.

- The present subject-matter is either known from D1 or is an obvious variation of the subject-matter of D1-D3 since it discloses dosage forms which are the mere combination of individual technical features known in the art of fighting involuntary movements, said dosage forms showing no unexpected technical effect: It is known that hydroxypropylmethylcellulose (HPMC) of the present examples impart delayed release properties when used as an ingredient of solid dosage forms.

Re Item VI

Document D4 has been published after the priority date of present application. It cannot be considered as relevant in the examination procedure of the PCT chapter II but may be used in the regional phase of the PCT against the novelty of the present subject-matter.

Re Item VIII

1. The term "release-retarding agent" used in claims 1 and 48-49 is vague and unclear and leaves the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of said claims unclear, Article 6 PCT. There is no definition of said term in reference books such as encyclopedias, dictionaries, teaching manuals and textbooks.

2. Independently of point 1 above, claim 1 does not meet the requirements of Article 6 PCT because the matter for which protection is sought is not clearly defined. With a comparison with a vague immediate release composition the claim attempts to define the subject-matter in terms of the result to be achieved, which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result.

3. Claim 19 does not meet the requirements of Article 6 PCT because the matter for which protection is sought is not clearly defined. With the wording "that exhibits a food effect", the claim attempts to define the subject-matter in terms of the result to be achieved, which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result.

4. The term "about" used in claims 10, 12, 14, 16-18 and 23 is vague and unclear and leaves the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of said claim unclear, Article 6 PCT.

5. The term "ng.hr/mL" used in claim 25 is vague and unclear and leaves the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of said claim unclear, Article 6 PCT. It seems that the matter for which protection is sought is not clearly defined. The claim attempts to define the subject-matter in terms of the result to be achieved, which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result.

6. Claims 26-27 do not meet the requirements of Article 6 PCT because the matter for which protection is sought is not clearly defined. The claims attempt to define the subject-matter in terms of the result to be achieved, which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result. Moreover, said claims relate to a statistical data, an AUC, which cannot be used for limiting a subject-matter of a claim in view of the inherent variability of said number among living species.

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